HIV in Adolescents and Young Adults

Introduction

Background

Adolescence and young adulthood is a period of intense physical and developmental transition that is characterized by experimentation and self-discovery. Adolescents and young adults with HIV in the United States primarily represent two distinct groups based on when and how they acquired HIV: (1) those who acquired HIV through perinatal transmission and now have reached the age of adolescence or young adulthood, and (2) those who acquired HIV during adolescence or young adulthood through sexual contact or drug use. In addition, rare cases of HIV acquisition occur in childhood as a result of child sexual abuse. In the United States, since the contemporary perinatal HIV transmission rate has been reduced to less than 1% of pregnancies in women with HIV, most adolescents and young adults with HIV have acquired HIV via sexual activity. Adolescents and young adults, particularly individuals from racial, ethnic, gender and sexual minority groups, comprise almost a quarter of new HIV diagnoses in the United States.

Definition of Adolescents and Young Adults

In the Centers for Disease Control and Prevention (CDC) surveillance reports, adolescents are defined as persons 13 to 19 years of age and young adults are defined as persons 20 to 24 years of age, unless otherwise specified. The Adult and Adolescent ARV Guidelines define adolescents as postpubertal youth who have a sexual maturity rating of IV or V (Table 1).

HIV Care Cascade/HIV Care Continuum

Limited data exist regarding the HIV care cascade (or HIV care continuum) outcomes in adolescents and young adults in the United States. In a sample from 1,411 adolescents and young adults with HIV aged 12-24 years at 13 United States urban HIV care centers as part of the SMILE collaborative project, 75% were linked to care, 59% were engaged in care, 34% were actually retained in care, and only 12% had suppressed HIV RNA levels. In 2016 end-of-year estimates based on CDC surveillance data, among persons with HIV aged 13-24 years, the overall rates of virologic suppression were only 30%, and there were major drop-offs from those projected to be living with HIV to those diagnosed, linked, and retained in care. In both of these analyses, younger populations with HIV had disproportionately lower rates of viral suppression than rates typically reported in adults.

Health Care for Adolescents and Young Adults with HIV
Despite steps in the right direction, there is a relative lack of data on the needs of adolescents and young adults with HIV, and more research is needed to develop optimal strategies for engaging, diagnosing, and managing this population.\[12,13\] Optimal care should include a medical provider with adolescent expertise and a clinic environment that incorporates a youth medical home model that can foster trust and maintain confidentiality (Figure 3).\[14,15\] This Topic Review will address routine care for adolescents and young adults with HIV, adolescent sexuality and reproductive health, transitioning from adolescent to adult care, and preexposure prophylaxis in adolescents and young adults ages 25 years and older.
Epidemiology of HIV in Adolescents and Young Adults

2014 HIV Surveillance Case Definition

The CDC established the first HIV surveillance case definition in 1982, with major revisions released in 1987, 1993, 2008, and most recently in 2014. The 2014 case definition establishes criteria for confirming a diagnosis of HIV infection, including laboratory and clinical evidence, as well as criteria for classifying the stage of HIV infection (stage 0, 1, 2, 3, or unknown).[16] The following summarizes recent HIV surveillance data in adolescents and young adults.

Adolescents and Young Adults with Diagnosed HIV

At year-end 2018, there were 31,900 adolescents and young adults (age 13 to 24 years) with diagnosed HIV in the United States.[17] Adolescents and young adults together comprised a small fraction (3.1%) of the total number of persons living with diagnosed HIV in the United States at year-end 2018 (Figure 4).[17] In contrast, adolescents and young adults accounted for a substantial proportion (20.8%) of persons with newly diagnosed HIV in 2018 (Figure 5).[17] By year-end 2018, the rate per 100,000 population of new HIV diagnoses was 0.2 for adolescents 13-14 years of age, 8.1 for adolescents 15-19 years, and 27.9 for young adults (ages 20-24 years).[17] From 2014-2018, the number of annual new HIV diagnoses remained relatively stable for adolescents (ages 13-19 years), but consistently declined for young adults (ages 20 to 24 years) (Figure 6).[17]

Race/Ethnicity

In 2018, among the 31,893 adolescents and young adults living with diagnosed HIV in the United States, 18,122 (56.8%) were black/African American, 7,269 (22.8%) Hispanic/Latinx, and 4,432 (13.9%) white (Figure 7).[17] In addition, the 2018 rates of diagnosed HIV in the United States, for age groups 13-14, 15-19, and 20-24 years were by far the highest in black/African Americans than any other racial/ethnic group (Figure 8).[17] In 2018, among the 7,817 new HIV diagnoses in adolescents and young adults, 4,104 (52.5%) were black/African-American, 1,9648 (24.9%) were Hispanic/Latinx, and 1,335 (17.1%) were white (Figure 9).[17]

Geographic Region

In 2016, among the 35,075 adolescents and young adults with diagnosed HIV in the United States, 18,101 (51%) were living in the South, 6,539 (19%) in the Northeast, 5,190 (15%) in the Midwest, and 5,245 (15%) in the West (Figure 10).[4] Among the 8,540 adolescents and young adults newly diagnosed with HIV infection in 2016, 4,606 (54%) were living in the South, which was at least 3-fold greater than any other region.[18]

Transmission Categories

The following summarizes HIV transmission category data in the United States for adolescents and young adults, for those living with diagnosed HIV in 2016 and those newly diagnosed HIV infections in 2017.[4] These data indicate two different HIV populations in adolescents and young adults—those acquired through perinatal transmission and those who acquired HIV as adolescents through sex or injection drug use.[4]

- **HIV Infection by Sex**: For the 35,075 persons aged 13 to 24 years living with diagnosed HIV, 27,384 (78%) were male and 2,048 (22%) were female.[4] Among those newly diagnosed with HIV in 2017, 7,167 (87%) were male and 1,042 (13%) were female.[4]
- **Males Aged 13 to 19 Years**: In 2016, for males 13 to 19 years of age living with diagnosed HIV, 55% acquired HIV via male-to-male sex, 35% by perinatal transmission, 2% by heterosexual sex, 2% by injection drug use and male-to-male sex, less than 1% by injection drug use alone, and 5% by other routes.[4]
• **Females Aged 13 to 19 Years**: For females aged 13 to 19 years living with diagnosed HIV, 66% acquired HIV through perinatal transmission, 21% by heterosexual sex, 2% by injection drug use, and 11% via other routes.[4]

• **Males Aged 20 to 24 Years**: For males 20 to 24 years of age living with diagnosed HIV, 85% acquired HIV through male-to-male sex, 7% through perinatal transmission, 3% by heterosexual sex, 3% by injection drug use and male-to-male sex, 1% by injection drug use alone, and less than 1% by other routes.[4]

• **Females aged 20 to 24 Years**: For this age group living with diagnosed HIV, 58% acquired HIV through heterosexual sex, 33% from perinatal transmission, 7% by injection drug use, and 3% via other routes.[4]
Testing, Linkage to Care, and Retention in Care

CDC HIV Testing Recommendations for Adolescents and Young Adults

Since 2006, the CDC has recommended opt-out HIV testing for all persons between the ages of 13 and 64, unless the local prevalence of undiagnosed HIV infection has been documented to be less than 0.1%. Accordingly, routine HIV screening should include adolescents and young adults. Testing should be performed annually (or more frequently) for individuals at higher risk of acquiring HIV—defined by CDC as persons who use injection drugs (and their sex partners), persons who exchange sex for money or drugs, sex partners of persons with HIV, and men who have sex with men, or heterosexual persons who themselves or whose sex partners have had more than one sex partner since their most recent HIV test. In addition, the CDC and the United States Public Services Task Force (USPSTF) recommend performing HIV testing whenever an acute sexually transmitted infection is diagnosed. Suboptimal HIV testing rates in vulnerable, at-risk youth, translate into missed opportunities for HIV prevention and HIV treatment in these youth.

HIV Risk and HIV Testing Rates

In the United States, multiple sources and studies have shown that many adolescents and young adults regularly engage in sexual activity that could place them at risk of acquiring HIV.

- **Youth Risk Behavior Surveillance System**: Data from the Youth Risk Behavior Surveillance System has demonstrated that among high school students in 2017, 39.5% reported having sexual intercourse at least once, 28.7% were sexually active, 46.2% reported condomless sex at last intercourse, and 9.7% reported having had 4 or more lifetime sex partners. This same report noted that 13% of students who had sexual contact with a person of the opposite sex were tested for HIV and 20% of students who had sexual contact with same or both sexes were tested for HIV.

- **CDC HIV Testing Services Data**: In addition, a separate report found 22% of high school students who had ever had sexual intercourse had ever been tested for HIV and only 33% of young adults (aged 18 to 24 years) had ever been tested for HIV.

- **Philadelphia Health System STI Study**: In a retrospective analysis of 1,313 adolescents and young adults aged 13 to 24 years seen in 2 urban primary care clinics in Philadelphia, investigators reported that only 55% of visits for an acute sexually transmitted infection episode were associated with a completed HIV test.

Knowledge of HIV Status

Based on estimates from CDC surveillance data and estimates in 2018, adolescents and young adults with HIV have the lowest awareness of their HIV diagnosis among any age group—45% of them were unaware of their HIV diagnosis; by comparison, among all people with HIV in 2018, an estimated 13.8% were unaware of their HIV diagnosis.

Point-of-Care Rapid HIV Testing

A systematic review of 14 studies evaluating the use of rapid point-of-care HIV testing found conclusive evidence that adolescents and young adults accept and prefer point-of-care rapid HIV testing platforms compared with traditional laboratory testing. Avoiding venipuncture and obtaining results faster were key reasons that rapid testing was preferred, and the review also found that adolescents and young adults were likely to accept rapid testing when offered rather than having to ask for the test. There are, however, several caveats with point-of-care testing. First, most point-of-care tests have lower sensitivity than currently used laboratory-based HIV-1/2 antigen-antibody tests, particularly with respect to diagnosing acute HIV. Second, any positive point-of-care test will require a blood draw for confirmatory HIV testing. Last, many office settings do not have trained staff to perform point-of-care testing and obtaining a blood draw for a laboratory-based test is usually much more efficient.
Barriers to HIV Testing in Adolescents and Young Adults

The reasons for the discordance between HIV risk behavior and HIV testing rates in youth are myriad and include lack of knowledge about HIV risk, lack of perceived risk, sense of invulnerability to disease, lack of access to (or awareness of) free and confidential HIV testing sites, stigma, and misconception that parental consent is required for HIV testing. Additional HIV testing barriers that have been identified are lack of medical provider awareness that CDC HIV testing recommendations include testing of adolescents and young adults, lack of medical insurance, and overall limited engagement with health systems. Educating pediatricians and primary care medical providers about HIV testing recommendations for adolescents and young adults has the potential to increase HIV testing, especially given that a private physician office or other clinic site is still the most likely setting for adolescents and young adults to get HIV testing, with fewer than 5% undergoing HIV testing at a designated HIV testing site. In Connect to Testing and Prevention Services, a demonstration study conducted by the Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN), investigators evaluated strategies for increasing HIV testing among sexual minority males aged 13 to 24 years. Based on their findings, they concluded that universal HIV screening of adolescents and young adults may play an important role in reducing stigma, but this approach may not adequately reach populations, such as youth of color, at high risk for acquiring HIV. Specifically, they found a community-based, targeted HIV testing approach was more effective than routine screening for sexual minority males aged 13 to 24 years.

Factors Impacting Linkage and Engagement in Care

For persons diagnosed with HIV, linkage to care within 30 days of diagnosis, and retention in HIV clinical care are associated with improved clinical outcomes, decreased mortality, and decreased HIV transmission to sex and injecting-drug partners. Although significant research has been conducted on interventions to improve linkage to care for persons newly diagnosed with HIV infection, few studies have included adolescents and young adults. Therefore, the individual and structural barriers for linkage to care and engagement in HIV care that are unique to adolescents and young adults remain poorly defined. Adolescents and young adults with HIV may struggle to navigate complex medical systems, especially as they transition from pediatric to adult health centers; during this transition many adolescents and young adults lack full autonomy as they remain dependent on their families for health insurance, transportation, housing, and other needs. For those young adults who become infected with HIV while on a parental insurance plan, inadvertent disclosure of their HIV status may occur. Adolescents and young adults who are members of racial, ethnic, gender, or sexual minorities may face additional stigma. In addition, receiving an HIV diagnosis during the vulnerable period spanning adolescence and early adulthood can lead to higher rates of depression and anxiety that may serve as barriers to engagement in care.

Strategies for Improving Linkage to Care and Retention in Care

Interventions to improve engagement along every step of the HIV care continuum include the following: adolescent-targeted (or adolescent-friendly) services include providing dedicated adolescent-only office hours; screening for sexually transmitted infections (of genital and extragenital sites); providing condoms and hormonal contraceptives; offering preexposure prophylaxis and nonoccupational postexposure prophylaxis; connecting to peer educators and adolescent support groups; and linkage to care specialists and intensive case management.
Clinical and Laboratory Monitoring

Baseline Evaluation for Newly Diagnosed Adolescents or Young Adults

For an adolescent or young adult newly diagnosed with HIV, the goals of the initial evaluation are the same as for adults and are outlined by the Adult and Adolescent ARV Guidelines: confirm the diagnosis of HIV, obtain a complete medical history, perform a physical examination, obtain relevant laboratory data, screen for sexually transmitted infections (at genital and extragenital sites of exposure), screen for substance use disorders, provide education about HIV, and link to appropriate primary care resources if necessary.[33] For younger adolescents, additional psychosocial intervention and additional education may be necessary, and this should ideally involve the parents or guardians, though this depends on multiple factors, including state law, institutional policy, maturity of the adolescent, and social situation. The initial evaluation of persons newly diagnosed with HIV is discussed in detail in the Initial Evaluation Topic Review in the Basic Primary Care module.

Routine Monitoring

Routine laboratory and clinical monitoring of adolescents and young adults with HIV is the same as for adults with HIV and is outlined in the antiretroviral therapy guidelines.[34]
Antiretroviral Therapy for Adolescents with HIV

Initiating Antiretroviral Therapy for Adolescents and Young Adults

All adolescents and young adults with HIV should receive antiretroviral therapy, regardless of their CD4 cell count or HIV RNA level.[2] Teenagers or young adults who acquired HIV via perinatal transmission have typically been on antiretroviral therapy for many years prior to reaching adolescence, and they often have complex antiretroviral regimens as a result of antiretroviral resistance mutations that accumulated over the many preceding years of receiving antiretroviral therapy.[35,36,37] All youth who acquire HIV as a teenager or young adult should be started on antiretroviral therapy (if not already receiving it). Prior to initiating antiretroviral therapy, careful attention should be given to the readiness of the adolescent or young adult to start antiretroviral therapy, including assessment for adherence and screening for mental health and substance use disorders.[2] In addition, reproductive health issues should be addressed prior to starting antiretroviral therapy. Standard baseline laboratory testing, including an HIV drug resistance genotype, should be ordered prior to starting antiretroviral therapy.

Choosing Antiretroviral Therapy Regimens

The selection and dosing of antiretroviral medications for adolescents is based on sexual maturity rating, rather than on age. The recommended antiretroviral regimens for initial therapy for post-pubescent adolescents whose sexual maturity rating is IV or V, and for all young adults, are the same as the Adult and Adolescent ARV Guidelines (Table 2) and (Table 3).[38] For pre-pubescent adolescents with sexual maturity ratings between I and III, separate Pediatric ARV Guidelines are available to guide the antiretroviral regimen selection and medication dosing (Table 4).[39]

Special Considerations for Persons of Childbearing Potential

The Adult and Adolescent ARV Guidelines provides recommendations on the use of dolutegravir and other integrase strand transfer inhibitors (INSTIs) in persons of child-bearing potential (Table 5).[38] These recommendations were updated due to additional data from the Botswana study that showed a 0.3% prevalence of neural tube defects in infants who were exposed to dolutegravir at the time of conception; the 0.3% prevalence of neural tube defects was slightly higher than the 0.1% observed in infants who were exposed to antiretroviral medications that did not include dolutegravir at the time of conception.[38]

Laboratory Monitoring after Starting Antiretroviral Therapy

Routine laboratory and clinical monitoring of adolescents and young adults after starting antiretroviral therapy is the same as for adults with HIV and is outlined below.[34,42] The following summarizes recommendations in the Adult and Adolescent ARV Guidelines for monitoring HIV RNA levels and CD4 cell counts after starting antiretroviral therapy:

- **HIV RNA Monitoring:** All individuals initiating antiretroviral therapy should have a baseline HIV RNA level and a repeat level obtained 2-8 weeks after initiating therapy. Subsequently, HIV RNA levels should be repeated every 4-8 weeks until the viral load is suppressed. Once HIV RNA levels are suppressed, monitoring should be done every 3-4 months. For adherent patients who have consistently suppressed HIV RNA levels and stable immunologic status for at least 2 years, HIV RNA monitoring can be extended to 6-month intervals. If a patient has a change in clinical status or has to initiate therapy with chronic corticosteroids, chemotherapy, or interferon, the HIV RNA levels should be checked every 3 months.

- **CD4 Cell Count:** All persons starting on antiretroviral therapy should have a baseline CD4 cell count and a repeat value 3 months after starting therapy. During the first 2 years on antiretroviral therapy the CD4 count should be monitored every 3-6 months. After 2 years on antiretroviral therapy, for adherent patients who have consistently suppressed HIV RNA levels, the frequency of CD4 cell count
monitoring can be based on CD4 cell count: (1) if the CD4 count is less than 300 cells/mm$^3$, monitoring should continue every 3-6 months, (2) if the CD4 count is consistently in the 300 to 500 cells/mm$^3$ range, monitoring can be extended to 12-month intervals, and (3) if the CD4 count is consistently greater than 500 cells/mm$^3$, monitoring may then be considered optional. If a patient has an increase in HIV RNA, a change in clinical status, or has to initiate therapy with immunosuppressive medications, such as corticosteroids, biologics, or chemotherapy, the CD4 cell count levels should be checked every 3-6 months.
Adherence to Antiretroviral Therapy

Challenges with Adherence to Antiretroviral Therapy

Poor adherence to antiretroviral therapy reduces the likelihood of virologic suppression, increases the risk of developing drug resistance mutations and virologic failure, limits future treatment options, and can lead to both disease progression and HIV transmission due to uncontrolled viremia. As a group, adolescents and young adults with HIV struggle with adherence more than their adult counterparts and have lower rates of viral suppression and higher rates of viral rebound. Multiple studies have identified several important barriers to antiretroviral medication adherence for adolescent populations, including depression, disruption of daily routine, poor understanding of the importance of adherence, denial and fear, forgetfulness, comorbid mental health diagnoses, substance use, lack of family and social support, and structural barriers such as homelessness. In a study of adherence in youth (aged 12 to 24 years) with either perinatal HIV acquisition (“perinatal group”) or HIV acquisition through sexual activity or drug use, the two groups in the study had many overlapping adherence challenges, but also had distinct reasons for having problems with adherence.[43] “Forgetting” to take the medication was by far the most common adherence barrier in both groups.[45] Overall, the barriers were greater in the perinatal group and these youth were more likely to report side effects from medications (likely due to higher pill burden and prior medication exposure).[45] In general, adolescents may be especially sensitive to side effects.[2]

Strategies for Improving Antiretroviral Adherence in Adolescents

The Pediatric ARV Guidelines outline recommendations for adherence monitoring (Table 7).[47] In addition, these guidelines provide strategies for improving adherence that are focused on initial intervention strategies, medication strategies, and follow-up intervention strategies (Table 8).[47] In some studies, reminder systems, such as cell phone calls, alerts, and text messaging, have been found to be particularly effective for adolescents and young adults.[2,45] Studies that have evaluated the usage of mobile phone and text messaging interventions to assist with medication adherences have found mixed results, depending on the measured outcome and the specific technology that was used.[48,49,50,51] In general, technologies involving two-way communication seemed to yield better antiretroviral adherence outcomes compared to stand-alone short message service (SMS) text message reminders.[50,51] For adolescents who continue to struggle with adherence despite multidisciplinary approaches, antiretroviral therapy may need to be temporarily discontinued to avoid inducing antiretroviral drug resistance. In these situations, when an antiretroviral regimen is restarted, it should include medications with high genetic barriers to resistance.
Preexposure Prophylaxis (PrEP) for Adolescents

Preexposure prophylaxis (PrEP) is an important prevention strategy for persons who are at high risk of acquiring HIV, with several landmark clinical trials demonstrating safety and efficacy in preventing HIV acquisition in men who have sex with men (MSM) and in men and women in heterosexual HIV-serodifferent couples.[52,53,54,55,56] Most of these trials included a significant proportion of young adults aged 18-24 years in the patient population enrolled, but very few included adolescents (age younger than 18 years). On the basis of these study results, the U.S. Public Health Service issued clinical practice guidelines for the use of PrEP in May 2014 and these guidelines were updated in March 2018.[57,58]

Major PrEP Studies in Adolescents and Young Adults

Two major trials have been conducted examining the safety and efficacy of tenofovir DF-emtricitabine for PrEP in adolescents and young adults in the United States.

- **ATN 113**: The Adolescent Trials Network 113 (ATN 113) study enrolled 260 adolescent males aged 15 to 17 years who have sex with other males in cities across the United States.[59] In this study, tenofovir DF-emtricitabine PrEP was found to be safe and well-tolerated, but adherence to PrEP, based on tenofovir diphosphate levels in dried blood spots, decreased markedly over time (Figure 13).[59] The HIV seroconversion rate was 6.4 per 100 person-years high and an incidence of sexually transmitted infections of 18 per 100 person-years.[59]

- **ATN 110**: The Adolescent Trials Network 110 (ATN 110) study enrolled 400 adolescent males (aged 18 to 22 years who have sex with other males) between March and September 2013.[60] Using tenofovir diphosphate levels in dried blood spots as a marker for adherence with PrEP, the investigators concluded there was a major decline in adherence at week 24.[60] The rates of STIs were high at baseline line (22% of participants) and remained high throughout the study.[60]

Legal Issues Related to PrEP and Minors

All states and the District of Columbia permit minors to consent for testing and treatment of sexually transmitted infections without parenteral consent and many explicitly designate HIV as a sexually transmitted infection in the law with respect to parental consent.[61] In addition, 9 states have laws that provide minors with broad authority to consent to any health care service or procedure, but these state laws have different age cutoffs and criteria (e.g. homelessness, living separate or apart from parents, and/or managing own financial affairs) for minor to be granted this authority.[61] No states have a law that prohibits a minor from granting autonomous consent for preexposure prophylaxis. From a practical standpoint, it may be very difficult for a minor to maintain the confidentiality of their receipt of PrEP from their parents (if on the parent’s health insurance plan), since many states allow medical providers to disclose the minor’s treatment information to the parents and billing services often include information in the explanation of benefits and specific charges that would reveal receipt of PrEP clinical services and medications for PrEP.[61]

Recommendations for Preexposure Prophylaxis in Youth

For young adults aged 18 to 24 years at risk for HIV infection, guidelines for PrEP are the same as adults at risk for acquiring HIV.[57,58] Because large randomized studies of PrEP did not involve persons under the age of 18, there is no formal guidance regarding use of PrEP in adolescents.[60] Nevertheless, based on findings from ATN 113, in May 2018, the United States FDA approved tenofovir DF-emtricitabine for PrEP in adolescents at risk for HIV who weigh at least 35 kilograms (77 pounds). In addition, based on results from the DISCOVER trial, the FDA has approved tenofovir alafenamide-emtricitabine for PrEP in men who have sex with men and for transgender women; the same minimum weight of 35 kg is required.[62] With the potential of PrEP use in adolescents, infrastructure for coordinated delivery of HIV prevention services for adolescents are needed that include HIV testing programs that link at-risk youth who test HIV negative to PrEP services.[28,63]
Immunizations for Adolescents with HIV

General Principles for Vaccine Administration in Youth with HIV

The Advisory Committee on Immunization Practices (ACIP) publishes separate annual guidelines for the use of vaccines in children and adolescents (birth to 18 years) and for adults (age 19 and older), with both guidelines including routine immunization schedules based on medical and other conditions.[64,65,66,67] The following discussion provides additional details for some of the immunizations in adolescents and young adults. All inactivated vaccines are considered safe to administer to adolescents and young adults with HIV, irrespective of immune status. The ACIP recommends that all adolescents with HIV through 18 years of age should receive most vaccines per standard recommended (or catch-up) schedules, with the following major exceptions:[65,66]

1. Precaution should be used when administering rotavirus vaccine,
2. The measles-mumps-rubella (MMR) and varicella vaccines are contraindicated if the CD4 percentage is less than 15 or the CD4 count is less than 200 cells/mm\(^3\), and
3. Modified dosing schedules are required for Haemophilus influenzae type b, pneumococcal conjugate and polysaccharide, meningococcal ACWY, and human papilloma virus (HPV) vaccines.

Human Papillomavirus (HPV) Vaccine

The ACIP recommends routinely administering a 3-dose series of the 9-valent HPV vaccine (9vHPV) for all males and females with HIV who are aged 11 to 26 years; the series may be started as early as 9 years of age (and should be started at age 9 in children with a history of sexual abuse or assault).[66] All adolescents and young adults with HIV should receive the 3-dose 9vHPV vaccine series, regardless of the age when the HPV vaccine series is started.[65,66,68] For pregnant individuals who have not received a complete HPV immunization series, the vaccine series initiation (or series completion) should be deferred until after pregnancy.[64]

Influenza

Annual inactivated influenza vaccine is recommended for all adolescents and young adults, including those with HIV and regardless of CD4 cell count.[64,65,66,67] The recombinant influenza vaccine should not be administered to persons younger than 18 years of age. The live attenuated influenza vaccines should not be administered to any person with HIV.[66,67]

Meningococcal ACWY Vaccine

For the general pediatric and adolescent population, the quadrivalent conjugate meningococcal vaccination is recommended beginning at age 11 or 12.[65] Either the MenACWY-D or MenACWY-CRM can be used as the conjugate meningococcal vaccine, but the same product should ideally be used for all doses.[65,66] For older adolescents and young adults who have not previously received the conjugate quadrivalent meningococcal vaccine, a two-dose initial series should be given 8 to 12 weeks apart.[69] The MenACWY-D vaccine should be given at least 4 weeks after completion of the conjugate pneumococcal vaccine series.[66] The following summarizes meningococcal ACWY vaccine booster dose recommendations for children, adolescents, and young adults with HIV.[66,69]

- A booster dose is also recommended every 5 years for adolescents and young adults who received the conjugate vaccine as a child.
- If the initial meningococcal series was administered prior to age 7, then the first booster dose should be given 3 years after completing the primary series and then subsequent booster doses given every 5 years.
- If the child was age 7 or older when the primary series was given, then the first booster dose should
be given 5 years after the primary series was completed and then subsequent booster doses should be given every 5 years.

**Meningococcal B Vaccine**

The serogroup B conjugate meningococcal vaccine is considered an optional vaccine for healthy youths 16-23 years of age and giving the vaccine should be based on shared decision-making; if given, the preferred age range is 16-18 years. There are no specific recommendations for administration of meningococcal B vaccine for persons with HIV infection. The ACIP recommends administering meningococcal B vaccine to all persons 10 years of age and older, with or without HIV, who have increased risk of meningococcal B disease (e.g. persistent complement component deficiencies, anatomic or functional asplenia, or receipt of a complement inhibitor, such as eculizumab or ravulizumab). Two meningococcal B vaccines are available: MenB-FHbp and MenB-4C. The ACIP does not give preference of one vaccine over the other, but the same vaccine must be used for all doses in the vaccine series. For persons with HIV, the dosing schedule for MenB-FHbp is a 3-dose series administered at 0, 1-2, and 6 months) and for MenB-4C a 2-dose series should be administered at 0 and 6 months. There are no recommendations to give booster doses for the meningococcal B vaccine.

**Pneumococcal Vaccine**

The ACIP recommends that all adolescents and young adults with HIV be given pneumococcal vaccine starting at entry into HIV care, according to the following strategy regarding the 13-valent pneumococcal conjugate (PCV13) and the 23-valent pneumococcal polysaccharide vaccine (PPSV23): If neither PCV13 nor PPSV23 has been received previously, administer 1 dose of PCV13 now and 1 dose of PPSV23 at least 8 weeks later. One additional dose of PPSV23 should be given 5 years after the first dose of PPSV23, and then again at age 65. If PCV13 has been received previously but PPSV23 has not, administer 1 dose of PPSV23 at least 8 weeks after the most recent dose of PCV13. One additional dose of PPSV23 should be given 5 years after the first dose of PPSV23, and again at age 65. If PPSV23 has been received but PCV13 has not, administer 1 dose of PCV13 at least 8 weeks after the most recent dose of PPSV23. One additional dose of PPSV23 should be given 5 years after the first dose of PPSV23, and again at age 65. Note the recommendation to administer PCV13 at least 8 weeks after the most recent dose of PPSV23 is for adolescents aged 18 years and younger with HIV. For persons with HIV who are older than 18 years of age, the ACIP recommends waiting at least 1 year after the most recent PPSV23 before giving the PCV13 dose. There are no recommendations to give booster doses for the pneumococcal vaccine.

**Varicella Vaccine**

Because varicella vaccine is a live attenuated vaccine, adolescents and young adults with HIV should not receive this vaccine if their CD4 count is less than 200 cells/mm$^3$. The following summarizes recommendations for administering varicella vaccine to nonimmune adolescents and young adults.

- Adolescents and young adults without evidence of varicella immunity and who have a CD4 count of 200 cells/mm$^3$ or greater should receive two doses of the single antigen varicella vaccine administered subcutaneously, 4 to 8 weeks apart. If more than 8 weeks elapses after the first vaccine dose, the second dose should be administered without restarting the schedule. All adolescents and young adults who receive varicella vaccine should be instructed to return promptly for evaluation if they develop a varicella-like rash following receipt of the vaccine.
Adolescent Sexuality, Gender, and Reproductive Health

Sexual Activity

Adolescence is often a period of heightened sexual and drug activity, which has significant implications for adolescents and young adults with HIV and for those at risk of acquiring HIV. In general, individuals who acquired HIV as an adolescent or young adult had an earlier onset of sexual activity than similarly aged adolescents and young adults who acquired HIV perinatally. In the LEGACY Study, the Longitudinal Epidemiologic Study to Gain Insight into HIV/AIDS in Children and Youth (LEGACY) evaluated 752 adolescents and young adults (aged 13 to 24 years) with HIV at 22 clinics in the United States and found that a significantly higher percentage of youth who acquired HIV as an adolescent or young adult were sexually active when compared with youth who acquired HIV perinatally (89.5% versus 34.1%), and had higher rates of sexually transmitted infections (32.1% versus 10.3%).

In the IMPAACT P1074 observational cohort study, analysis of 1,042 adolescents and young adults (ages 13-24 years) showed higher rates of sexually transmitted infections associated with non-perinatally HIV acquisition. In the Adolescent Medicine Trials Network, investigators analyzed cross sectional survey data between 2009–2012 collected from 2,198 youth with HIV aged 12 to 26 years at 20 ATN sites; those who acquired HIV as adolescents and young adults had a higher number of recent sex partners and more episodes of condomless sex with serodifferent partners when compared with those with perinatally acquired HIV.

Screening for Sexually Transmitted Infections

All adolescents and young adults with HIV should undergo screening for sexually transmitted infections according to the 2015 Sexually Transmitted Diseases Treatment Guidelines. These guidelines recommend screening for sexually transmitted infections in all sexually active persons with HIV at the initial HIV care visit and at least annually thereafter. Specific screening should be performed at genital and extragenital sites for curable sexually transmitted diseases (e.g. syphilis, gonorrhea, and chlamydia). For those with ongoing sexually transmitted infection risk, screening (at genital and/or extragenital sites of exposure) are recommended once every 3 to 6 months.

Contraceptive Management

Sexually active adolescent and young adult women with HIV should have access to the same array of contraceptive options as older women with HIV, including hormonal contraception (e.g. pill, ring, injection, or implant) and intrauterine devices (IUDs). Significant drug interactions can occur between hormonal contraceptives and certain antiretroviral medications; these interactions are detailed in the Adult and Adolescent ARV Guidelines in the table on Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives. The CDC has published the U.S. Medical Eligibility Criteria for Contraceptive Use (US MEC), which provides specific guidance regarding hormonal contraceptive use for women at high risk for acquiring HIV. These guidelines take into consideration the available data related to HIV acquisition or transmission associated with hormonal contraception use and the benefits of preventing unintended pregnancy. A full discussion of contraceptive management for HIV in persons with HIV is available in a separate Topic Review.

Sexual Minority Adolescents and Young Adults Infected With HIV

Gay, bisexual, and other young men who have sex with men (YMSM), particularly those who are black, have a disproportionate burden of youth with HIV in the United States and require additional psychosocial and
healthcare interventions. Moreover, young sexual minority (those who do not identify as heterosexual) males are less likely than young women and heterosexual males to be receiving antiretroviral therapy. Information on gender identity is not consistently collected or documented in current HIV surveillance systems, but studies have reported a high HIV prevalence among transgender persons (approximately 20 to 30%), particularly among transgender women. Sexual and gender minority adolescents and young adults with HIV are more likely to have a lower education level, lower perceived risk, and lower levels of family and social support, as well as structural barriers to accessing healthcare, such as discrimination and decreased access to identity-affirming healthcare clinics and providers.
Special Considerations for Youth with Perinatal HIV

Informing Children and Adolescents of Their HIV Status

For children who have acquired HIV perinatally, the timing of informing them of their HIV status is a highly sensitive and complicated issue. Studies of youth who acquire HIV perinatally found 10 years of age was the typical time for informing a youth of their HIV status, which is older than for many other chronic conditions.[76] The LEGACY study that included 571 youth with perinatally-acquired HIV found that 32% of those aged 13 years and older were unaware of their HIV status and 25% of those unaware of HIV status were sexually active.[76] Lack of knowledge of HIV status as a young person who is entering adolescence is problematic and has obvious implications for HIV transmission.[76,88] The American Academy of Pediatrics strongly encourages disclosure of HIV to school-aged children and states that adolescents should know their HIV status and be informed about the consequences of their health behaviors, including sexual activity.[89]

MENTAL HEALTH

Adolescents and young adults who acquired HIV perinatally have higher rates of mental health conditions disorders with peers without HIV, as shown in one study that found a 12-month psychiatric disorder prevalence of nearly 70% among adolescents and young adults with HIV (or with a history of exposure to HIV).[90] An extensive literature review further confirmed the high prevalence rates of psychiatric disorders in youth with HIV.[91] According to a review of 8 small studies involving youth with HIV (who acquired HIV perinatally), the most common mental disorders were attention deficit hyperactivity disorder (28.6%), anxiety (24.3%), and depression (25%).[92] Youth with perinatally acquired HIV may also have high rates of behavioral, developmental, and neurocognitive disorders.[93,94] Anxiety, depression, substance use, and post-traumatic stress disorder are common among youth with HIV who acquired HIV as an adolescent or young adults.[95]
Transitioning to Adult Care

Transitioning from Adolescent to Adult Care

Adolescents and young adults with chronic diseases, including HIV, may face a difficult time in transitioning from adolescent to adult health care settings. The transition may be complicated by several different factors, including the presence of coexisting developmental or psychosocial delays, attachment to pediatric/adolescent providers, difficulty trusting a new provider, adjustment to an adult care setting that typically has less psychosocial support and allows less time per encounter, insurance and financial issues, and a lack of communication between pediatric and adult providers.[2,12,25,96,97,98] Medical providers and institutions transition youth to adult clinics at different ages (some at age 18, some at age 21, and some at age 24 or 25), so the maturity of the transitioning adolescent/young adult often varies in different health care settings. Adolescents with perinatal HIV may struggle with additional burdens, such as loss of a parent to HIV and stigma relating to their HIV diagnosis.[96,97] Because of these many factors, there is often a high rate of attrition, and potentially an increase in mortality among adolescents with HIV as they transition from the pediatric/adolescent multidisciplinary care setting to the adult medical care setting.[97,99]

Models of Transition to Adult Care

The concept of health care transition, which has been defined as the purposeful planned movement of children with special health needs from child-centered to adult-centered care, is a relatively new frontier for HIV medicine, since children with HIV did not typically survive to adulthood prior to the availability of effective antiretroviral therapy.[96,98,100] Researchers have found that an organized, deliberate, developmentally appropriate, and compassionate process of medical care transition can improve outcomes as adolescents and young adults enter adult care settings.[12,101] Adolescents and young adults should be included in the conversations around transition, as there are clear discrepancies between what adolescents and young adults need and expect from their medical home, and what they experience (Table 9). [15] Various facilitators to a successful transition have been identified, such as developing a relationship with the new adult provider prior to the actual transition, educating adult HIV care teams about transition, developing an individualized transition plan, and providing a formal written transition document. [2,12,96,97,101] There are, however, no evidenced-based guidelines or models to inform the type of transitional care that should be provided to adolescents and young adults with HIV.
Summary Points

- The HIV epidemic among adolescents and young adults encompasses two very different populations: those who acquired HIV perinatally (vertical transmission) and those who acquired HIV as adolescents or young adults through sex or injection drug use (horizontal or behavioral transmission).
- Adolescents and young adults in the United States comprised only 3% of persons with diagnosed HIV at year-end 2018; a disproportionate number of youth with HIV are African American or Hispanic/Latinx.
- In 2018, adolescents and young adults accounted for 21% of persons newly diagnosed with HIV and a disproportionate number of these new infections in youth were African American or Hispanic/Latino.
- Male-to-male sex represents the highest risk category for both adolescents and young adults.
- HIV testing rates are low among adolescents and young adults, and 45% of persons with HIV who are 13 to 24 years of age are unaware of their HIV diagnosis.
- All adolescents and young adults with HIV should receive antiretroviral therapy, both for their own health benefit and to reduce the risk of HIV transmission to others.
- For adolescents, antiretroviral therapy selection and dosing is based on sexual maturity rating rather than on age.
- Concerns about barriers to adherence with adolescents should not exclude youth from receiving antiretroviral therapy, but should prompt extra effort to prepare youth for starting antiretroviral therapy and to support adherence while on treatment.
- Most adolescents and young adults with HIV are sexually active, with higher rates of sexual activity reported among those who acquire HIV as adolescents compared with those who acquired HIV perinatally.
- Researchers have found that an organized, deliberate, culturally competent, developmentally appropriate, and compassionate process of transition can improve health outcomes as adolescents and young adults enter adult care settings, which is essential for their continued engagement in HIV.
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[PubMed Abstract] -  

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[PubMed Abstract] -  

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[PubMed Abstract] -  

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Figures

Figure 1 HIV Continuum of Care for Adolescents and Young Adults Attending 13 Urban US HIV Care Centers of the NICHD-ATN-CDC-HRSA SMILE Collaborative

Data from the Strategic Multisite Initiative for the Identification, Linkage, and Engagement in Care of HIV-infected youth (SMILE) were from October 2012-September 2014. Viral suppression (VS) was defined as at least 1 HIV viral load below the level of detection on study.

**Figure 2 HIV Continuum of Care for Youth Aged 13 to 24 Years, 2016**

Figure 3 Components of Youth Medical Home Model

Source: Tebb KP, Pica G, Peake K, Diaz A, Brindis CD. Adolescent and Health Professional Perspectives on the Medical Home: Improving Health Care Access and Utilization Under the Affordable Care Act: Philip R. Lee Institute for Health Policy Studies and Division of Adolescent and Young Adult Medicine, Department of Pediatrics, University of California, San Francisco; July 2016.
Figure 4 Persons Living with Diagnosed HIV in United States, by Age Group, Year-End 2018

Figure 5 New Diagnoses of HIV in United States by Age Group at Time of Diagnosis, United States, 2018

Figure 6 New Diagnoses of HIV in Adolescents and Young Adults, United States, 2014-2018

Figure 7 Adolescents and Young Adults with Diagnosed HIV in United States, by Race/Ethnicity, Year-End, 2018

Figure 8 Rate of Adolescents and Young Adults with Diagnosed HIV by Race/Ethnicity, United States, Year-End 2018


<table>
<thead>
<tr>
<th>Racial/Ethnic Group</th>
<th>Living with Diagnosed HIV (per 100,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age 13-14</td>
</tr>
<tr>
<td>American Indian/Alaska Native</td>
<td>0</td>
</tr>
<tr>
<td>Asian</td>
<td>8.2</td>
</tr>
<tr>
<td>Black/African American</td>
<td>38.2</td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>4.3</td>
</tr>
<tr>
<td>Native Hawaiian/Other Pacific Islander</td>
<td>12.0</td>
</tr>
<tr>
<td>White</td>
<td>2.0</td>
</tr>
<tr>
<td>Person of Multiple Races</td>
<td>8.0</td>
</tr>
</tbody>
</table>
Figure 9 New HIV Diagnoses in Adolescents and Young Adults, by Race/Ethnicity, United States, 2018

This graphic shows the estimated number of adolescents and young adults living with newly diagnosed HIV infection in the United States in 2018, based on race/ethnicity. Note the number of African-American youth newly diagnosed with HIV outnumbers whites by more than 3-fold.

Figure 10 Persons with Diagnosed HIV, Aged 13 to 24 Years, by Region of Residence, 2016

This graphic shows that among adolescents and young adults living with HIV in the United States, more reside in the South than any other region.

This graphic shows that among persons living with HIV, those aged 13-24 years have the highest percentage with undiagnosed HIV.

Figure 12 Youth Risk Behavior Survey (YRBS) HIV Test Settings for Young Adults Ever Tested for HIV

This graphic shows the test setting for young adults ever tested for HIV. The data was obtained from the National Youth Risk Behavior Survey (YRBS) and Behavioral Risk Factor Surveillance System (BRFSS). The setting where they were last tested was used if more than one HIV test had been obtained. Fewer than 5% were tested at an HIV testing site.

Figure 13 Tenofovir diphosphate Levels During 48 Weeks of PrEP in ATN 113 Study

Figure 14 Sexually Transmitted Infections in Youth in IMPAACT P1074

The International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) P1074 observational cohort study followed 1,042 adolescents and young adults ages 13-24 years and determined rates of sexually transmitted infections (STIs) and compared these rates based on mode of HIV acquisition.

Figure 15 Sexual Risk Behavior Among Youth with HIV Aged 12-26 Years in Adolescent Medicine Trial Network (ATN) Sites, 2009-2012

The Adolescent Medicine Trial Network (ATN) data was collected between 2009 and 2012 from 20 cross-sectional surveys completed by 649 youth with perinatally-acquired HIV and 1,547 youth with HIV acquired as an adolescent or young adult.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Female</th>
<th>Male</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Age Range (years)</td>
<td>Breast Growth</td>
</tr>
<tr>
<td>I</td>
<td>0-15</td>
<td>Pre-adolescent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Breast budding (t helarche); areolar hyperplasia with small amount of breast tissue</td>
</tr>
<tr>
<td>II</td>
<td>8-15</td>
<td>Further enlargement of breast tissue and areola, with no separation of their contours</td>
</tr>
<tr>
<td>III</td>
<td>10-15</td>
<td>Separation of contours; areola and nipple form secondary mound above breasts tissue</td>
</tr>
<tr>
<td>IV</td>
<td>10-17</td>
<td>Large breast with single contour</td>
</tr>
<tr>
<td>V</td>
<td>12.5-18</td>
<td></td>
</tr>
<tr>
<td>Stage</td>
<td>Female</td>
<td></td>
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<tr>
<td>-------</td>
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</tr>
<tr>
<td></td>
<td>Age Range (years)</td>
<td>Breast Growth</td>
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</tbody>
</table>

Source:

Table 2. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV

**Recommended Initial Regimens for Most People with HIV**

Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use (listed in alphabetical order).

### Integrase Strand Transfer Inhibitor + 2 Nucleoside Reverse Transcriptase Inhibitors:

**Note:** For individuals of childbearing potential, see the table Considerations Before Initiating one of these regimens.

- Bictegravir-tenofovir alafenamide-emtricitabine (AI)
- Dolutegravir-abacavir-lamivudine<sup>a</sup> (AI)—if HLA-B*5701 negative and without chronic hepatitis B coinfection
  - Dolutegravir plus tenofovir alafenamide<sup>b</sup>-emtricitabine (AI)
  - Dolutegravir plus tenofovir DF<sup>b</sup>-emtricitabine<sup>a</sup> (AI)
  - Raltegravir<sup>c</sup> plus tenofovir DF<sup>b</sup>-emtricitabine<sup>a</sup> (BI)
  - Raltegravir<sup>c</sup> plus tenofovir alafenamide<sup>b</sup>-emtricitabine (BII)

### Integrase Strand Transfer Inhibitor + 1 Nucleoside Reverse Transcriptase Inhibitor

- Dolutegravir-lamivudine (AI)—except for individuals with HIV RNA >500,000 copies/mL, HBV coinfection, or in whom antiretroviral therapy is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available

<sup>a</sup>Lamivudine may substitute for emtricitabine or vice versa, if a non-fixed dose NRTI combination is desired.

<sup>b</sup>Tenofovir alafenamide and tenofovir DF are two forms of tenofovir approved by the FDA. Tenofovir alafenamide has fewer bone and kidney toxicities than tenofovir DF, while tenofovir DF is associated with lower lipid levels. Safety, cost, and access are among the factors to consider when choosing between these drugs.

<sup>c</sup>Raltegravir can be given as 400 mg twice daily or 1200 mg (two 600-mg tablets) once daily; the once daily dosing should not be used in pregnant persons.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies; III = Expert opinion

Source:

Table 3. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV

Recommended Initial Regimens in Certain Clinical Situations

These regimens are effective and tolerable, but have some disadvantages when compared with the regimens listed above, or have less supporting data from randomized clinical trials. However, in certain clinical situations, one of these regimens may be preferred.

Integrase Strand Transfer Inhibitors + 2 Nucleoside Reverse Transcriptase Inhibitors:

Note: for individuals of childbearing potential, see the table Considerations Before Initiating Dolutegravir and Other Integrase Strand Transfer Inhibitors as Initial Therapy before prescribing one of these regimens.

- Elvitegravir-cobicistat-tenofovir alafenamide\(^b\)-emtricitabine (BI)
- Elvitegravir-cobicistat-tenofovir DF\(^b\)-emtricitabine (BI)

Boosted Protease Inhibitor plus 2 Nucleoside Reverse Transcriptase Inhibitors:\(^a\,\[^\]b\)

(in general, boosted Darunavir is preferred over boosted Atazanavir):

- Darunavir plus ritonavir plus tenofovir alafenamide\(^b\)-emtricitabine\(^a\) (AI)
- Darunavir plus ritonavir plus tenofovir DF\(^b\)-emtricitabine\(^a\) (AI)
- Darunavir-cobicistat plus tenofovir alafenamide\(^b\)-emtricitabine\(^a\) (AI)
- Darunavir-cobicistat plus tenofovir DF\(^b\)-emtricitabine\(^a\) (AI)
- Atazanavir plus ritonavir plus tenofovir alafenamide\(^b\)-emtricitabine\(^a\) (BI)
- Atazanavir plus ritonavir plus tenofovir DF\(^b\)-emtricitabine\(^a\) (BI)
- Atazanavir-cobicistat plus tenofovir alafenamide\(^b\)-emtricitabine\(^a\) (BI)
- Atazanavir-cobicistat plus tenofovir DF\(^b\)-emtricitabine\(^a\) (BI)
- Darunavir plus ritonavir plus abacavir-lamivudine\(^a\) (BII)—if HLA-B*5701 negative
- Darunavir-cobicistat plus abacavir-lamivudine\(^a\) (BII)—if HLA-B*5701 negative

Non-Nucleoside Reverse Transcriptase Inhibitor + 2 Nucleoside Reverse Transcriptase Inhibitors:

- Doravirine-tenofovir DF-lamivudine (BI)
- Doravirine plus tenofovir alafenamide-emtricitabine (BIII)
- Efavirenz (600 mg)-tenofovir DF-emtricitabine\(^a\) (BI)
- Efavirenz (400 mg)-tenofovir DF-emtricitabine\(^a\) (BI)
- Efavirenz (600 mg) plus tenofovir alafenamide-emtricitabine (BII)
- Rilpivirine-tenofovir DF\(^b\)-emtricitabine\(^a\) (BI)—if HIV RNA <100,000 copies/mL and CD4 count >200 cells/mm\(^3\)
- Rilpivirine-tenofovir alafenamide\(^b\)-emtricitabine\(^a\) (BI)—if HIV RNA <100,000 copies/mL and CD4 count >200 cells/mm\(^3\)

Regimens to Consider when Abacavir, Tenofovir alafenamide, and Tenofovir DF Cannot be Used or Are Not Optimal:

- Dolutegravir-lamivudine (AI), except for individuals with HIV RNA >500,000 copies/mL, HBV co-infection, or in whom antiretroviral therapy is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available
- Darunavir plus ritonavir plus raltegravir twice daily (CI)—if HIV RNA <100,000 copies/mL and CD4 count >200 cells/mm\(^3\)
- Darunavir plus ritonavir once daily plus lamivudine\(^a\) (CI)

\(^a\) Lamivudine may substitute for emtricitabine or vice versa, if a non-fixed dose NRTI combination is desired.

\(^b\) Tenofovir alafenamide and tenofovir DF are two forms of tenofovir approved by the FDA. Tenofovir alafenamide has fewer bone and kidney toxicities than tenofovir DF, while tenofovir DF is associated with lower lipid levels. Safety, cost, and access are among the factors to consider when choosing between these drugs.

\(^\wedge\) This regimen can also be given as the single-tablet darunavir-cobicistat-tenofovir alafenamide-emtricitabine...
These regimens are effective and tolerable, but have some disadvantages when compared with the regimens listed above, or have less supporting data from randomized clinical trials. However, in certain clinical situations, one of these regimens may be preferred.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies; III = Expert opinion

Source:

### Antiretroviral Regimens Recommended for Initial Therapy in Children

#### Preferred Regimens

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Regimen Options</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infants, Birth to &lt;14 Days</strong>&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>2NRTIs plus Nevirapine&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Children Aged ≥14 Days to &lt;3 Years</strong></td>
<td>2NRTIs plus Lopinavir-ritonavir&lt;br&gt;2NRTIs plus Raltegravir&lt;sup&gt;c&lt;/sup&gt; (weight ≥2 kg)</td>
</tr>
<tr>
<td><strong>Children Aged ≥3 Years (weight &lt;25 kg)</strong></td>
<td>2NRTIs plus Atazanavir plus Ritonavir&lt;br&gt;2NRTIs plus twice daily Darunavir&lt;sup&gt;d&lt;/sup&gt; plus Ritonavir</td>
</tr>
<tr>
<td><strong>Children Aged ≥3 Years (weight ≥25 kg)</strong></td>
<td>2NRTIs plus Dolutegravir&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Adolescents Aged ≥12 Years with SMRs 1-3 (weight ≥25 kg)</strong></td>
<td>2NRTIs plus Bictegravir&lt;sup&gt;g&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Adolescents Aged ≥12 Years with SMRs 4 or 5</strong></td>
<td>Refer to the Adult and Adolescent Antiretroviral Therapy Guidelines</td>
</tr>
</tbody>
</table>

#### Alternative Regimens

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Regimen Options</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Children Aged ≥14 Days to &lt;3 Years</strong></td>
<td>2NRTIs plus Nevirapine&lt;sup&gt;h&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Children Aged ≥3 Months to &lt;3 Years</strong></td>
<td>2NRTIs plus Atazanavir plus Ritonavir</td>
</tr>
<tr>
<td><strong>Children ≥3 Years (weight ≥20 kg to &lt;25 kg)</strong></td>
<td>2NRTIs plus Dolutegravir&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Children Aged ≥3 Years (weight ≥25 kg)</strong></td>
<td>2NRTIs plus Atazanavir plus Ritonavir&lt;br&gt;2NRTIs plus Darunavir plus Ritonavir&lt;sup&gt;d&lt;/sup&gt;&lt;br&gt;2NRTIs plus Raltegravir&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Children Aged ≥3 Years</strong></td>
<td>2NRTIs plus Efavirenz&lt;sup&gt;i&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Children Aged ≥6 Years to &lt;12 Years (weight ≥25 kg)</strong></td>
<td>2NRTIs plus Bictegravir&lt;sup&gt;g&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Adolescents Aged ≥12 Years with SMRs 1-3 and weight ≥35 kg</strong></td>
<td>2NRTIs plus Rilpivirine&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Adolescents Aged ≥12 Years with SMRs 1-3 and weight ≥40 kg</strong></td>
<td>2NRTIs plus Atazanavir-cobicistat</td>
</tr>
<tr>
<td><strong>Adolescents Aged ≥12 Years with SMRs 4 or 5</strong></td>
<td>Refer to the Adult and Adolescent Antiretroviral Therapy Guidelines</td>
</tr>
</tbody>
</table>

#### Preferred 2-NRTI Backbone Options for Use in Combination with Additional Drugs

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Regimen Options</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Children, Birth to Age &lt;3 Months</strong></td>
<td>Zidovudine plus (Lamivudine or Emtricitabine)</td>
</tr>
<tr>
<td><strong>Children Aged ≥3 Months and &lt;6 Years</strong></td>
<td>Abacavir plus (Lamivudine or Emtricitabine)&lt;sup&gt;m&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Children and Adolescents Aged ≥6 Years and SMR 1-3</strong></td>
<td>Tenofovir alafenamide-Emtricitabine (only if weight ≥25 kg and receiving a regimen that contains an integrase strand transfer inhibitor or a non-nucleoside reverse transcriptase inhibitor)&lt;sup&gt;o&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Adolescents Aged ≥12 Years and SMRs of 4 or 5</strong></td>
<td>Refer to Adult and Adolescent Antiretroviral Therapy Guidelines</td>
</tr>
</tbody>
</table>
Alternative 2-NRTI Backbone Options for Use in Combination with Additional Drugs

<table>
<thead>
<tr>
<th>Age/Group</th>
<th>Backbone (and Additional Drugs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children Age ≥3 Months</td>
<td>Zidovudine plus Abacavir</td>
</tr>
<tr>
<td>Children Age ≥2 Years to 12 Years</td>
<td>Tenofovir DF plus (Lamivudine or Emtricitabine)</td>
</tr>
<tr>
<td>Children and Adolescents Aged ≥6 Years and SMRs of 1-3</td>
<td>Zidovudine plus (Lamivudine or Emtricitabine)</td>
</tr>
</tbody>
</table>

If treatment initiation is planned prior to 14 days of age, nevirapine is the Preferred agent. However, there are currently no clinical trial data suggesting that initiating treatment within the first 14 days of life improves outcome (compared with starting after 14 days of age). Consultation with an expert in pediatric HIV infection should be sought. A change from nevirapine to lopinavir-ritonavir should be considered when the infant is aged ≥14 days and 42 weeks post-gestational age, based on infant genotype and the better outcomes of lopinavir-ritonavir in children aged <3 years.

Lopinavir-ritonavir should not be administered to neonates before a postmenstrual age (first day of the mother’s last menstrual period to birth plus the time elapsed after birth) of 42 weeks and postnatal age ≥14 days.

Raltegravir pills or chewable tablets can be used in children aged ≥2 years. Granules can be administered in infants and children aged 4 weeks to 2 years.

Darunavir should only be used in children weighing ≥10 kg. Once-daily darunavir should not be used in children aged <12 years or weighing <40 kg or if any one of the following resistance-associated substitutions are present: V11I, V32I, L33F, I47V, I50V, I54L, I54M, T74P, L76V, I84V, and L89V. Darunavir + ritonavir is an Alternative recommendation for children aged ≥6 years to <12 years and weighing ≥25 kg because there are options that can be administered once-daily. Note that darunavir plus ritonavir can be administered once daily in adolescents aged ≥12 years and weighing ≥40 kg who are not sexually mature (SMR 1-3).

A fixed-dose concentration tablet (dolutegravir-abacavir-lamivudine) is available for children who weigh ≥25 kg.

Elvitegravir is currently recommended only in fixed-dose combination tablets. Tablets containing elvitegravir-cobicistat-emtricitabine-tenofovir alafenamide are recommended as Preferred for children and adolescents weighing ≥25 kg.

Bictegravir is currently recommended only in fixed-dose combination tablets. Tablets containing bictegravir-emtricitabine-tenofovir alafenamide are recommended as Preferred regimen for adolescents aged ≥12 years and weighing ≥25 kg and as an Alternative regimen for children aged ≥6 and weighing ≥25 kg.

Nevirapine should not be used in post-pubertal girls with CD4 counts >250/mm³, unless the benefit clearly outweighs the risk. Nevirapine is approved by the FDA for treatment of infants aged ≥15 days.

Efavirenz is licensed for use in children aged ≥3 months who weigh ≥3.5 kg but is not recommended by the Panel as initial therapy in children aged ≥3 months to 3 years.

Rilpivirine should be administered to adolescents aged ≥12 years and weighing ≥35 kg who have an initial viral load ≤100,000 copies/mL.

Darunavir-cobicistat is available as part of a fixed-dose combination tablet containing darunavir-cobicistat-emtricitabine-tenofovir alafenamide that has been approved by the FDA for use in children and adolescents weighing ≥40 kg.

A fixed-dose combination tablet that contains zidovudine-lamivudine is available for use in children weighing ≥30 kg.
A fixed-dose combination tablet that contains abacavir-lamivudine is available for use in children weighing ≥25 kg.

Tenofovir alafenamide-emtricitabine plus a boosted protease inhibitor is only recommended for use in children and adolescents weighing ≥35 kg.

Source:

- Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the use of antiretroviral agents in pediatric HIV infection. What to start: regimens recommended for initial therapy of antiretroviral-naive children. April 14, 2020. [HIV.gov]
Considerations Before Initiating Dolutegravir and Other Integrase Strand Transfer Inhibitors (INSTIs) as Initial Therapy for Persons of Child-Bearing Potential

Before Initiating an INSTI-Containing Regimen in a Person of Childbearing Potential:

- A pregnancy test should be performed (AIII).
- To enable individuals of childbearing potential to make informed decisions, providers should discuss the benefits and risks of using dolutegravir around the time of conception, including the low risk of neural tube defects and the relative lack of information on the safety of using other commonly prescribed antiretroviral drugs, including other INSTIs, around the time of conception (AIII).
- **For individuals who are trying to conceive**, the Panel recommends initiating one of the following regimens, which are designated as Preferred regimens during pregnancy in the Perinatal Guidelines: use of an anchor drug (raltegravir, or atazanavir boosted with ritonavir, or darunavir boosted with ritonavir) plus a 2-drug backbone (tenofovir DF-emtricitabine, or tenofovir DF plus lamivudine, or abacavir-lamivudine). Dolutegravir would be an Alternative, rather than a Preferred, option (BII).
- **For individuals who are not planning to conceive but who are sexually active and not using contraception**, consider a regimen’s effectiveness and tolerability, the available data on potential teratogenicity, and the person’s preferences (e.g. low pill burden) when choosing among regimens recommended for initial therapy. In this situation, dolutegravir would be an Alternative, rather than Preferred, option (BII). If the person becomes pregnant, changes to the antiretroviral regimen may be warranted. In this situation, clinicians should refer to the Perinatal Guidelines or recommendations.
- **For individuals who are using effective contraception**, a dolutegravir-based regimen is one of the recommended options; however, clinicians should discuss the risks and benefits of using dolutegravir with patients to allow them to make an informed decision (AIII).
- An approach similar to that outlined for dolutegravir should be considered for bictegravir-containing antiretroviral therapy (AIII).
- Regimens that contain elvitegravir-cobicistat should not be used during pregnancy because of inadequate drug concentrations of elvitegravir in the second and third trimesters (AII).
- Clinicians should refer to the Perinatal Guidelines when prescribing antiretroviral therapy for a pregnant person with HIV.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies; III = Expert opinion
Source:

Table 6.

**Barriers to Medication Adherence, by Route of Infection: Youth Aged 12 to 24**

<table>
<thead>
<tr>
<th>Barriers Reported by Participants</th>
<th>Perinatal HIV Infection, % (n = 217)</th>
<th>Youth HIV Infection, % (n = 236)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forgot</td>
<td>75.1</td>
<td>72.9</td>
</tr>
<tr>
<td>Didn’t feel like taking it, needed a break&lt;sup&gt;a&lt;/sup&gt;</td>
<td>39.2</td>
<td>22.0</td>
</tr>
<tr>
<td>Taking it reminds me a of HIV, want to forget&lt;sup&gt;a&lt;/sup&gt;</td>
<td>35.5</td>
<td>21.6</td>
</tr>
<tr>
<td>Made me sick to my stomach/tasted bad&lt;sup&gt;a&lt;/sup&gt;</td>
<td>27.6</td>
<td>14.4</td>
</tr>
<tr>
<td>Ran out of prescription</td>
<td>17.5</td>
<td>21.2</td>
</tr>
<tr>
<td>Worried someone would find out about HIV</td>
<td>16.1</td>
<td>19.9</td>
</tr>
<tr>
<td>Got in the way of my daily schedule</td>
<td>17.5</td>
<td>14.4</td>
</tr>
<tr>
<td>Family and/or friends don’t help me remember</td>
<td>17.5</td>
<td>12.3</td>
</tr>
<tr>
<td>Got another illness, wasn’t feeling well</td>
<td>14.7</td>
<td>10.6</td>
</tr>
<tr>
<td>Change in living situation, moved</td>
<td>8.8</td>
<td>12.7</td>
</tr>
<tr>
<td>Can’t get pill at drug store</td>
<td>9.2</td>
<td>12.7</td>
</tr>
<tr>
<td>Get sick even when I take the pills&lt;sup&gt;a&lt;/sup&gt;</td>
<td>14.7</td>
<td>6.4</td>
</tr>
<tr>
<td>Don’t understand why have to take the pills</td>
<td>11.5</td>
<td>5.5</td>
</tr>
<tr>
<td>Nowhere to keep pills at school or work&lt;sup&gt;b&lt;/sup&gt;</td>
<td>11.1</td>
<td>5.9</td>
</tr>
<tr>
<td>Didn’t think I need the pills anymore&lt;sup&gt;a&lt;/sup&gt;</td>
<td>12.0</td>
<td>4.2</td>
</tr>
<tr>
<td>Did not have health insurance</td>
<td>6.0</td>
<td>6.8</td>
</tr>
<tr>
<td>Got a headache, other physical symptom</td>
<td>6.0</td>
<td>6.8</td>
</tr>
<tr>
<td>Family or friends say I shouldn’t take them</td>
<td>1.4</td>
<td>2.1</td>
</tr>
<tr>
<td>Other</td>
<td>22.6</td>
<td>24.2</td>
</tr>
</tbody>
</table>

<sup>a</sup>Percentage of participants endorsing significantly different by route of infection, p ≤.01
<sup>b</sup>Percentage of participants endorsing significantly different by route of infection, p ≤.05

Acknowledgment: This table has been reprinted with permission from Springer Nature: AIDS and Behavior.

Source:

### Table 7. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

**Evidence-Based Approaches for Monitoring Medication Adherence**

<table>
<thead>
<tr>
<th>Routine Assessment of Medication Adherence in Clinical Care</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monitor viral load.</td>
<td>Viral load monitoring should be done more frequently after initiating or changing medications</td>
</tr>
<tr>
<td>Assess quantitative self-report of missed doses.</td>
<td>Ask patient and/or caregiver about the number of missed doses over defined period (1, 3, or 7 days).</td>
</tr>
<tr>
<td>Elicit description of medication regimen.</td>
<td>Ask patient and/or caregiver about the name/appearance, number, frequency of medications.</td>
</tr>
<tr>
<td>Assess barriers to medication administration.</td>
<td>Engage the patient and caregiver in dialogue around facilitators and challenges to adherence.</td>
</tr>
<tr>
<td>Monitor pharmacy refills.</td>
<td>Approaches include pharmacy-based or clinic-based assessment of on-time medication refills.</td>
</tr>
<tr>
<td>Conduct announced and unannounced pill counts.</td>
<td>Approaches include asking patients to bring medications to clinic, home visits, or referral to community health nursing.</td>
</tr>
</tbody>
</table>

**Targeted Approaches to Monitor Adherence in Special Circumstances**

<table>
<thead>
<tr>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implement directly observed therapy.</td>
</tr>
<tr>
<td>Measure plasma drug concentration.</td>
</tr>
</tbody>
</table>

**Approaches to Monitor Medication Adherence in Research Settings**

<table>
<thead>
<tr>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measure drug concentrations in hair.</td>
</tr>
<tr>
<td>Use mobile phone-based technologies.</td>
</tr>
</tbody>
</table>

**Source:**

- Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the use of antiretroviral agents in pediatric HIV infection. Adherence to antiretroviral therapy in children and adolescents living with HIV. April 14, 2020. [HIV.gov]
Table 8. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

### Strategies for Improving Adherence to Antiretroviral Medications

<table>
<thead>
<tr>
<th>Initial Intervention Strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Establish trust and identify mutually acceptable goals for care.</td>
</tr>
<tr>
<td>• Obtain explicit agreement on the need for treatment and adherence.</td>
</tr>
<tr>
<td>• Identify depression, low self-esteem, substance abuse, or other mental health issues in the child/adolescent and/or caregiver that may decrease adherence. Evaluate and initiate treatment for mental health issues before starting antiretroviral drugs, if possible.</td>
</tr>
<tr>
<td>• Determine whether the child is aware of their HIV status. Consider talking to the child’s caregivers about disclosing this information to the child in a developmentally appropriate way.</td>
</tr>
<tr>
<td>• Identify family, friends, health team members, and others who can support adherence.</td>
</tr>
<tr>
<td>• Educate patient and family about the critical role of adherence in therapy outcome including the relationship between partial adherence and resistance and resistance and potential impact on future drug regimen choices. Develop a treatment plan that the patient and family understand and to which they feel committed.</td>
</tr>
<tr>
<td>• Work with the patient and family to make specific plans for taking medications as prescribed and supporting adherence. Assist them to arrange for administration in day care, school, and other settings, when needed. Consider home delivery of medications.</td>
</tr>
<tr>
<td>• Establish readiness to take medication through practice sessions or other means.</td>
</tr>
<tr>
<td>• Schedule a home visit to review medications and determine how they will be administered in the home setting.</td>
</tr>
<tr>
<td>• Consider a brief period of hospitalization at start of therapy in...</td>
</tr>
</tbody>
</table>
selected circumstances for patient education and to assess tolerability of medications chosen.

### Medication Strategies

- Choose the simplest regimen possible, reducing dosing frequency and number of pills.
- When choosing a regimen, consider the daily and weekly routines and variations in patient and family activities.
- Choose the most palatable medicine possible (pharmacists may be able to add syrups or flavoring agents to increase palatability).
- Choose drugs with the fewest adverse effects; provide anticipatory guidance for management of adverse effects.
- Simplify food requirements for medication administration.
- Prescribe drugs carefully to avoid adverse drug-drug interactions.
- Assess pill-swallowing capacity and offer pill-swallowing training and aids (e.g., pill swallowing cup, pill glide). Adjust pill size as needed.

### Follow-Up Intervention Strategies

- Have more than one member of the multidisciplinary team monitor adherence at each visit and in between visits by telephone, email, text, and social media, as needed.
- Provide ongoing support, encouragement, and understanding of the difficulties associated with maintaining adherence to daily medication regimens.
- Use patient education aids including pictures, calendars, and stickers.
- Encourage use of pill boxes, reminders, alarms, and timers.
- Provide follow-up clinic visits, telephone calls, and text messages to support and assess adherence.
- Provide access to support groups, peer groups, or one-on-one counseling for caregivers and patients, especially for those with known depression or drug use issues that are known to decrease
adherence.

- Provide pharmacist-based adherence support, such as medication education and counseling, blister packs, refill reminders, automatic refills, and home delivery of medications.
- Consider directly observed therapy at home, in the clinic, or in selected circumstances, during a brief inpatient hospitalization.
- Consider gastrostomy tube use in selected circumstances.
- Information on other interventions to consider can be found at [http://www.cdc.gov/hiv/prevention/research/compendium/ma/complete.html](http://www.cdc.gov/hiv/prevention/research/compendium/ma/complete.html)

Source:

- Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the use of antiretroviral agents in pediatric HIV infection. Adherence to antiretroviral therapy in children and adolescents living with HIV. April 14, 2020. [HIV.gov]
<table>
<thead>
<tr>
<th>What Adolescents Want</th>
<th>What Adolescents Experience</th>
</tr>
</thead>
</table>
| **Relationship with primary care provider who:** | • Lack of an established primary care provider  
• Lack of understanding and respect from their primary care provider  
• Barriers to accessing a primary care provider  
• Insufficient opportunities to talk with primary care provider |
| Knows them and cares about their health; | • Concerns about privacy and sharing information between providers  
• Limited selection of providers and care |
| Responds to them as individuals and treats them with respect; | Comprehensive care where physical, mental, vision and dental health care needs are met. |
| Can be accessed on a regular basis; and | Confidentiality assurances and protections |
| Can talk to about issues that are important to adolescents. | • Lack of knowledge of existing confidentiality rights and protections for adolescents  
• Barriers to having time alone with primary care providers |

Source:

- Tebb KP, Pica G, Peake K, Diaz A, Brindis CD. Adolescent and Health Professional Perspectives on the Medical Home: Improving Health Care Access and Utilization Under the Affordable Care Act: Philip R. Lee Institute for Health Policy Studies and Division of Adolescent and Young Adult Medicine, Department of Pediatrics, University of California, San Francisco; July 2016. [Health Policy Brief]